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Case Report

Reactive lymphoid hyperplasia in the oral cavity of a cardiac patient – case report

Gabriela Vieira Gomes [1,*], Lilia Timerman [2], Valéria Cristina de Souza [3]

[1] Resident of the Dentistry Center of the Multiprofessional Residency in Cardiovascular Health, Instituto Dante Pazzanese de Cardiologia, São Paulo, Brazil.
[2] Assistant Dental Surgeon, Department of Dentistry, Instituto Dante Pazzanese de Cardiologia, São Paulo, Brazil.
[3] Head Dental surgeon of the Dentistry Section, Instituto Dante Pazzanese de Cardiologia, São Paulo, Brazil.

* Correspondence: gabriela.gomes@dantepazzanese.org.br

Abstract: This descriptive observational study reports a case of reactive lymphoid hyperplasia in the oral cavity of a pediatric cardiac patient followed up at a public tertiary care hospital. This male patient was five years old, with hypoplastic left heart syndrome, treated with Carvedilol, Furosemide, Losartan, Warfarin, Montelukast, and beclometasone. His legal guardian reported an increased amount of tissue on the floor of the mouth ongoing for approximately 24 hours, followed by prostration, fever, bilateral lymphadenopathy, and a refusal to eat. After removal of the oral infectious foci (carious lesions) in the operating room, regression of the lesion and symptoms was observed, suggesting a diagnosis of a lesion caused by reactional lymphoid hyperplasia, a rare and benign condition in which there is an increase in tissue volume, caused by the proliferation of lymphoid cells to fight an aggressor agent.

Keywords: Pseudolymphoma; Congenital Heart Defects; Lymphoid Tissue; Mouth.

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1. Introduction

Lymphoid tissue is present throughout the body and plays a vital role in the body's immune response [1]. When stimulated by an aggressor agent, it can promote an exaggerated response involving cell proliferation, causing an increase in tissue volume called reactive lymphoid hyperplasia, a rare and benign condition that may affect lymph nodes, Waldeyer's ring lymphoid tissue or lymphoid tissue aggregates in the oral cavity [1,2].

Clinically, it may present as a painless, unilateral, or bilateral growth nodule, similar in color to the mucosa and with well-defined borders. Although the development in the oral cavity is rare, there are cases described in the palate, tongue, and salivary glands [3,4,5,6]. The diagnosis is usually clinical, however, in cases where there is uncertainty about the diagnosis, biopsies can be performed to rule out a possible malignancy [5]. Histologically, layers of differentiated lymphocytes arranged in multiple germinal centers are observed [5]. Lesions of reactive lymphoid hyperplasia usually regress spontaneously after removal of the aggressor agent; however, surgical removal can also be performed [5].

Congenital heart defects are anatomical anomalies in the heart, which can cause anything from simple to serious changes in the functioning of the cardiac pump [7]. Children with heart disease are predisposed to poor oral health due to factors such as lack of parental knowledge about the importance of hygiene, negative behavior of the child, defects in dental anatomy and use of medications [7].

Here we report on a case of reactive lymphoid hyperplasia in the mouth of a 5-year-old patient with complex congenital heart disease, treated in the surgical center of the Dante Pazzanese Cardiology Institute (Instituto Dante Pazzanese de Cardiologia).

2. Case Report

This case study describes a 5-year-old male patient with asthma and hypoplastic left heart syndrome, a complex congenital heart disease characterized by underdevelopment of left heart structures. The patient was under pharmacological treatment with carvedilol (6mg/dose 12/12h – 0.6mg/kg/day), furosemide (0.5mg/kg/day), losartan (1.5mg/kg/day), warfarin (according to the prothrombin time), montelukast (4mg 1x/day), and beclometasone (50mcg 1x/day). The child's guardian reported an increase in tissue on the floor of the mouth, which had first appeared approximately 24 hours beforehand, accompanied by prostration, fever, bilateral lymphadenopathy, and a refusal to eat.

Intraoral clinical examination revealed a nodular and erythematous hyperplastic lesion located on the base of the tongue, which was sessile and painless to the touch, and which covered the entire floor of the oral cavity, with lobular projections along its entire length, as well as cavities in all deciduous teeth, with extensive destruction of the dental crown of the lower molars near the lesion (Figure 1).

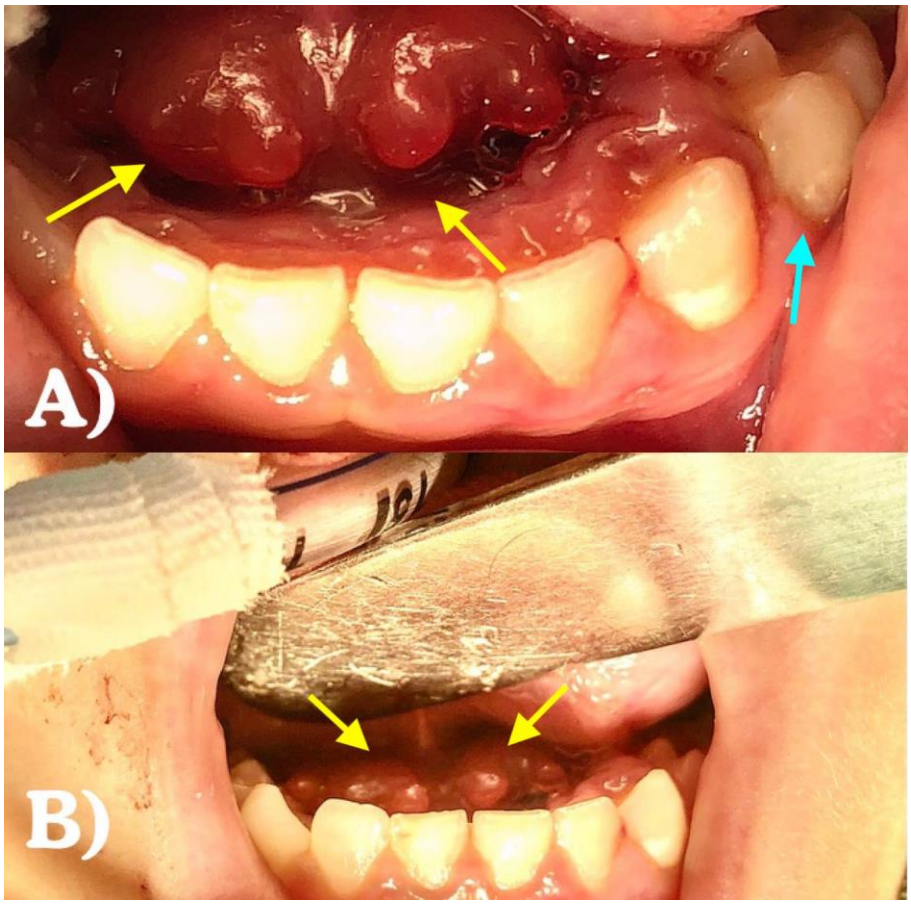

Figure 1. Nodular hyperplastic lesion on the base of the tongue covering the entire floor of the mouth, with a smooth surface, erythematous appearance, and lobular projections. A and B images show the intra and extraoral views, respectively. Yellow arrows indicate the hyperplastic lesion; blue arrow indicates caries in posterior teeth.

Extraoral physical examination showed bilateral cervical lymphadenopathy, more conspicuous on the left side, as well as flushing and increased local temperature, indicating an ongoing inflammatory process. Based on the information acquired in the anamnesis and clinical examination, the established diagnostic hypotheses included ranula, salivary duct cysts, and reactive lymphoid hyperplasia. The hypotheses relating to side effects of the administered drugs were discarded due to the rapid development of the lesion.

Due to the child's behavior, the number of dental procedures required, and the urgent need to perform cardiac surgery, the procedures related to cavity removal, restoration, and extraction were conducted in the operating room under general anesthesia. Intravenous corticosteroids (dexamethasone 2mg/ mL – 0.3mg/kg/day) were administered to avoid painful postoperative symptoms. No complications were reported during the procedures, with almost complete remission of the lesion observed a few hours after anesthetic recovery, which is characteristic of a lesion caused by reactive lymphoid hyperplasia (Figure 2).

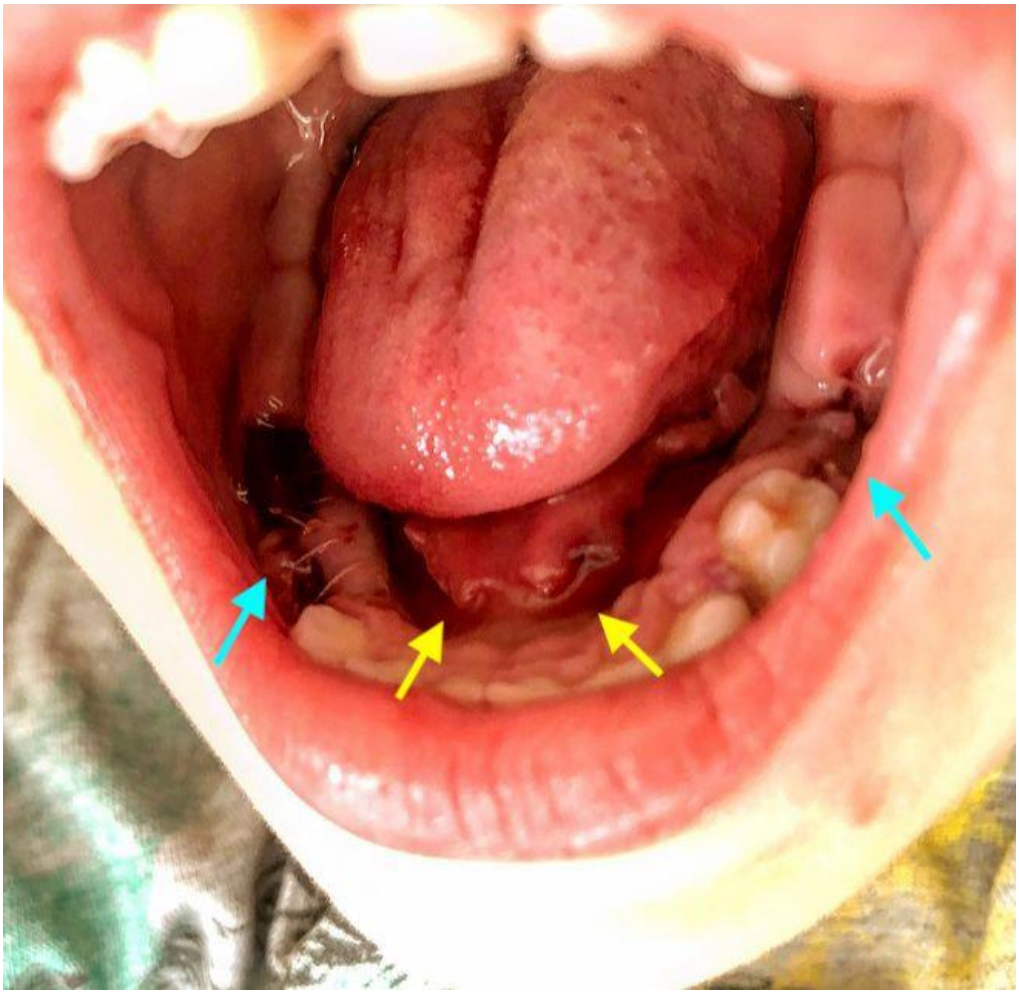

Figure 2. Almost complete remission of the lesion after removal of infectious foci due to carious lesions. Yellow arrows indicate reduction of the lesion; blue arrows indicate extractions performed.

The patient was discharged after three days in the hospital and medicated with amoxicillin and potassium clavulanate (400+57mg/ml – 50mg/kg/day) for seven days, as requested by the medical team. On his return two weeks after surgery, the echocardiography and laboratory tests were normal. The patient progressed well and was under

dental follow-up. A recommendation was made to the adult responsible for the patient to continue dental follow-up of the child every six months.

3. Discussion

Lymphoid tissue is spread as secondary lymphoid organs throughout the oral cavity and oropharynx and plays an essential role in the immune response [1]. This tissue is present in the soft palate, uvula, and pharynx, as well as, in smaller quantities and sizes, on the floor of the mouth, jugal mucosa, and tongue [1]. The tonsils are the main source of lymphoid tissue in the oral cavity, comprising clusters that defend the body against antigens from the air and food and which are more prominent in younger individuals [1]. To a lesser extent, other clusters of lymphoid tissue also play an essential role in combating aggressive antigens; their response to them depends on the type, intensity, and duration of the harmful stimulus [1]. As in other parts of the body, the lymphoid tissue of the oral cavity is highly reactive to harmful stimuli, causing cell proliferation and, consequently, an increase in local tissue volume (hyperplasia) [1]. Reactive lymphoid hyperplasia is one of the manifestations of this increase in tissue volume.

Neville et al. define reactive lymphoid hyperplasia as an increase in tissue volume caused by the proliferation of lymphoid cells to combat an aggressor agent. It may affect the lymph nodes, Waldeyer's ring lymphoid tissue, or lymphoid tissue aggregates that are typically spread throughout the oral cavity [2]. Usually, this tissue has a color similar to mucous membranes, or it may be dark pink if the lymphoid aggregate is deep inside the surrounding tissue or yellow/orange if it is closer to the surface [2]. The new tissue usually occurs symmetrical and bilaterally, differentiating it from malignant lesions [2]. Histologically, differentiated lymphocyte layers are observed with numerous collections of lymphoblasts, called germinal centers [2]. Diagnosis of this kind of lesion is usually clinical. However, if the appearance of the lesion resembles a lymphoma, biopsies may be requested to rule out malignant lesions in the soft palate region [2].

Adkins made the first record of reactive lymphoid hyperplasia in the oral cavity in 1973 [3]. Since then, few studies have reported this kind of lesion in the mouth, with most of these having been recorded on the palate and posterolateral region of the tongue. Despite the clinical similarity to other lesions, such as ranula (extravasation of saliva from the sublingual gland) and salivary duct cysts (non-neoplastic lesions that may obstruct the salivary ducts), some characteristic features lead to the diagnosis of reactive lymphoid hyperplasia [4].

The literature demonstrates that most of the lesions caused by reactive lymphoid hyperplasia do not require treatment, presenting spontaneous regression after removal of the aggressor stimulus [2]. Surgical removal of the lesions is only indicated in cases involving obstruction of the air passage, as in the case of lesions on the soft palate, tonsils, and posterior edges of the tongue [5-6]. The exact etiopathogenesis of reactive lymphoid hyperplasia is unknown. However, similar to other inflammatory conditions of the body, it is assumed that tissue inflammation caused by carious lesions promotes fluid accumulation and activation of phagocytic cells in the affected site, accompanied by an increase in levels of plasma proteins and neutrophilia [7]. The accumulation of exudate in the affected site is due to the increased blood flow and vascular permeability during the inflammatory process, which is essential to attract plasma components, such as macrophages and phagocytes, that assist in the elimination of pathogenic microorganisms [7]. In order to attract these plasma components, chemical mediators, such as cytokines and chemokines, need to be released, promoting and increasing expression of adhesion molecules and the recruitment of circulating leukocytes [7].

Hypoplastic left heart syndrome (HLHS) is a complex congenital heart disease characterized by underdevelopment (hypoplasia) of the structures on the left side of the heart (left ventricle, aorta, and aortic arch, besides to atresia or stenosis of the mitral valve). It can be diagnosed during pregnancy through echocardiography [8,9]. HLHS requires surgical correction, often performed during the first years of life, as it makes it harder to

pump blood to the rest of the body and is a risk to the patient's life [8,9]. No studies in the literature confirm the correlation between HLHS and infections in the oral cavity. However, it is known that patients with congenital heart diseases are at high risk of developing infectious processes on the surface of the endocardium [10], affecting the heart valves and causing infectious endocarditis. Endocarditis is a severe disease associated with bacteremia that may originate from dental procedures, and patients with poor oral health are at high risk [10,11]. Antibiotic prophylaxis is applied before dental procedures, such as tooth extractions and periodontal treatments, to reduce the bacterial load during the manipulation of oral tissues and prevent the development of infectious endocarditis of oral origin [11]. As antibiotic prophylaxis, this patient received IV cephalexin (50 mg/kg) one hour before the start of dental procedures [11].

The corticosteroid dexamethasone was intravenously administered to assist in the patient's full postoperative recovery. Dexamethasone is a synthetic glucocorticoid whose lipophilic nature allows it to cross the cell membrane and enter the cytoplasm rapidly. The dexamethasone molecule interacts with DNA to control inflammation by regulating the activation of different mediators and enzymes, such as cytokines, cyclooxygenase-2, and adhesion molecules [12].

In this case report, the lesion was observed to regress after the infections caused by the cavities were treated, suggesting that these extensive infection foci may have been the aggressive agent. However, the patient was treated with intravenous corticosteroids (dexamethasone 2mg/mL – 0.3mg/kg/day), which would also explain the rapid regression of the lesion. Based on the literature, it is thought that the principal reason the lesion regressed was the removal of harmful stimuli. This is the case even when the strong anti-inflammatory action of corticosteroids is considered, as the lesion did not return. Therefore, it is suggested that removing the infectious foci due to carious lesions was responsible for the regression of the lesion.

5. Conclusion

The diagnosis of lesions in the oral cavity is complex and can be hampered by anatomical variations and the broad spectrum of lesions. The established diagnostic hypotheses have in common an increase in tissue volume at the floor of the mouth, which is often painless. The reported case demonstrates the harmful potential of infectious foci in the mouth and the importance of oral health care, especially in patients with cardiovascular conditions.

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Supplementary Materials: None.

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